IN THE CLAIMS:

Please amend the claims, as follows.

Please amend claim 1, as follows:

Claim 1. (amended) A composition comprising:

(a) [an]a biologically active insulin-like growth factor-1 (IGF-I) or [an]a biologically active IGF-I analogue, wherein the IGF-I or IGF-I analogue is soluble in said composition at a concentration of at least about 12 mg/ml when said composition is at a temperature of about 4°C; and

(b) a solubilizing compound comprising a guanidinium group;

a1 wherein said IGF-I analogue is a compound selected from the group consisting of a compound that retains IGF-I activity, a compound that binds an IGF-I receptor, and a compound that retains IGF-I activity and binds an IGF-I receptor, and wherein said composition has a pH of at least about pH 5.5.

Claim 2. (amended) The composition of ~~claim~~ 1, wherein said solubilizing compound is arginine or an arginine analogue, wherein said arginine analogue is an amino acid analogue of arginine that increases solubility of IGF-I at a pH of about 5.5 or greater.

Please amend claim 5, as follows:

Claim 5. (amended) The composition of claim [1]4, wherein said solubilizing compound is present in a molar concentration range from about 15 mM to about 500 mM.

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Please amend claim 6, as follows:

Claim 6. (amended) The composition of claim [1]5, wherein said solubilizing compound is present in a molar concentration range from about 20 mM to about 200 mM.

Please amend claim 8, as follows:

Claim 8. (amended) The composition of claim [1]7, wherein said pH is in a range from about pH 5.7 to about pH 6.3.

Please amend claim 9, as follows:

Claim 9. (amended) The composition of claim [1]8, wherein said pH is about pH 6.0.

Please amend claim 11, as follows:

Claim 11. (amended) The composition of claim [1]10, wherein said IGF-I or IGF-I analogue is present in said composition in a concentration of about 15 mg/ml to about 200 mg/ml.

Please amend claim 12, as follows:

Claim 12. (amended) The composition of claim [1]11, wherein said IGF-I or IGF-I analogue is present in said composition in a concentration of about 25 mg/ml to about 200 mg/ml.

Please amend claim 15, as follows:

Claim 15. (amended) A composition comprising:

(a) [an]a biologically active insulin-like growth factor-1 (IGF-I) or [an]a biologically active IGF-I analogue, wherein the IGF-I or IGF-I analogue is soluble in said composition at a concentration of at least about 12 mg/ml when said composition is at a temperature of about 4°C;

(b) a solubilizing compound selected from the group consisting of arginine, an arginine analogue, and guanidine hydrochloride; and

(c) a buffer such that the composition has a pH of about pH 5.5 to about pH 9.0; wherein said IGF-I analogue is a compound selected from the group consisting of a compound that retains IGF-I activity, a compound that binds an IGF-I receptor, and a compound that retains IGF-I activity and binds an IGF-I receptor, and wherein said arginine analogue is an amino acid analogue of arginine that increases solubility of IGF-I at a pH of about 5.5 or greater.

Please amend claim 17, as follows:

Claim 17. (amended) A method of making an IGF-I composition comprising:

(a) providing an amount of [an]a biologically active insulin-like growth factor-1 (IGF-I) or [an]a biologically active IGF-I analogue such that the IGF-I or IGF-I analogue is soluble in said composition at a concentration of at least about 12 mg/ml when said composition is at a temperature of about 4°C; and

(b) combining the IGF-I or IGF-I analogue with a solubilizing compound comprising a guanidinium group; wherein the pH of the composition is about pH 5.5 to about pH 9.0;

wherein said IGF-I analogue is a compound selected from the group consisting of a compound that retains IGF-I activity, a compound that binds an IGF-I receptor, and a compound that retains IGF-I activity and binds an IGF-I receptor.

Please amend claim 20, as follows:

Claim 20. (amended) A method of enhancing the solubility of [an]a biologically active insulin-like growth factor-1 (IGF-I) or [an]a biologically active IGF-I analogue in a composition having a pH of about pH 5.5 to about 9.0, said method comprising combining said IGF-I or [an]said IGF-I analogue with an amount of a solubilizing compound that comprises a guanidinium group sufficient to increase the solubility of said IGF-I or [the]said IGF-I analogue relative to the solubility of said IGF-I or [the]said IGF-I analogue in the absence of the solubilizing compound, wherein said IGF-I analogue is a compound selected from the group consisting of a compound that retains IGF-I activity, a compound that binds an IGF-I receptor,

and a compound that retains IGF-I activity and binds an IGF-I receptor, and wherein said arginine analogue is an amino acid analogue of arginine that increases solubility of IGF-I at a pH of about 5.5 or greater.

Please add the following new claims:

--21. A method for stablizing solubility of a biologically active insulin-like growth factor-1 (IGF-I) or biologically active IGF-I analogue within an aqueous solution during freeze-thaw of said solution, said method comprising

a) preparing said solution; and

b) including arginine or an arginine analogue in said solution in an amount sufficient to stablize solubility of said IGF-I or IGF-I analogue within said solution during freeze-thaw relative to the solubility of IGF-I or the IGF-I analogue in the absence of arginine in said solution;

wherein said IGF-I analogue is a compound selected from the group consisting of a compound that retains IGF-I activity, a compound that binds an IGF-I receptor, and a compound that retains IGF-I activity and binds an IGF-I receptor, and wherein said arginine analogue is an amino acid analogue of arginine that increases solubility of IGF-I at a pH of about 5.5 or greater.

22. The method of claim 21, wherein said IGF-I or said IGF-I analogue is soluble in said solution at a concentration of about 7.4 mg/ml when said solution is at about 4°C, and wherein said arginine or arginine analogue is present in said solution at a concentration of about 50 mM.

23. A method for stabilizing biological activity of a biologically active insulin-like growth factor-1 (IGF-I) or biologically active IGF-I analogue in a composition during storage of said composition prior to its use, said composition having a pH of about pH 5.5 to about 9.0, said method comprising:

a) combining said IGF-I or said IGF-I analogue with an amount of a solubilizing compound in an amount sufficient to increase the solubility of said IGF-I or said IGF-I analogue relative to the solubility of said IGF-I or said IGF-I analogue in the absence of said solubilizing compound; and

b) storing said composition prior to its use.

24. The method of claim 23, wherein said solubilizing compound is arginine or an arginine analogue, wherein said arginine analogue is an amino acid analogue of arginine that increases solubility of IGF-I at a pH of about 5.5 or greater.

25. The method of claim 23, wherein said composition is a solution.

26. The method of claim 25, wherein said storing is at a temperature of about 2°C to about 8°C.

27. The method of claim 23, wherein said composition is a freeze-dried composition.

28. The method of claim 27, wherein said storing is at room temperature.--

REMARKS

Claims 1, 2, 5, 6, 8, 9, 11, 12, 15, 17, and 20 have been amended. Claims 21-28 have been added. Support for amendments to the claims and for newly added claims resides throughout the specification, particularly at pages 5, 6, 7, 10, 12, and 19. Claims 1-28 are pending. The Examiner's remarks in the Official Action are addressed below in the order set forth therein.

Specifically, claims 1, 2, 15, 17, and 20 have been amended in response to a rejection under 35 U.S.C. §112, second paragraph as being indefinite. Claims 5, 6, 8, 9, 11, and 12 have